

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/005140

International filing date (day/month/year)
08.12.2004

Priority date (day/month/year)
08.12.2003

International Patent Classification (IPC) or both national classification and IPC
G01N33/48, C07H21/00, C07D207/46, C07D207/44, C07K17/06

Applicant
OXFORD GENE TECHNOLOGY IP LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1 (a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Bardili, W

Telephone No. +49 89 2399-2132



Box No. 1 Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 6,7

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 6,7

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	30-42
	No: Claims	1-4,8-29
Inventive step (IS)	Yes: Claims	
	No: Claims	1-4, 8-42
Industrial applicability (IA)	Yes: Claims	1-4,6-42
	No: Claims	5

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 6, 7 and the corresponding dependent claims comprise numerous compounds comprised in the state of the art. The search and examination for this subject-matter is therefore incomplete.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- D1: NEUMANN W P ET AL: "STERICALLY HINDERED FREE RADICALS. 14. SUBSTITUENT-DEPENDENT STABILIZATION OF PARA-SUBSTITUTED TRIPHENYLMETHYL RADICALS" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, US, vol. 108, no. 13, 1986, pages 3762-3770, XP002265819 ISSN: 0002-7863
- D2: GILDEA B D ET AL: "A VERSATILE ACID-LABILE LINKER FOR MODIFICATION OF SYNTHETIC BIOMOLECULES" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 31, no. 49, 26 November 1990 (1990-11-26), pages 7095-7098, XP000172821 ISSN: 0040-4039
- D3: LEIKAUF E ET AL: "A COMBINATORIAL PROTECTING GROUP STRATEGY FOR OLIGONUCLEOTIDE SYNTHESIS" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 52, no. 20, May 1996 (1996-05), pages 6913-6930, XP002042681 ISSN: 0040-4020
- D4: SEIO, K. ET AL.: "Enhanced stereoselectivity in internucleosidic bond formation by the use of the chiral ribose moiety of thymidine" J. ORG. CHEM., vol. 68, 2003, pages 3849-3859, XP002328262
- D5: SCHIRRMACHER, R.: "Radiosynthesis of 2-(((4-(-2-(18F)fluoroethoxy)phenyl)bis(4-methoxy-phenyl)methoxy)ethyl)piperidine-3-carboxylic acid: a potential GAT-3-PET ligand to study GABAergic neurotransmission in vivo" J. RADIOLABEL. COMPOUNDS AND RADIOPHARM., vol. 44, 2001, pages 627-642, XP002328263

- D6: SHCHEPINOV, M.S. AND KORSHUN, V.A.: "Recent applications of bifunctional trityl groups" CHEM. SOC. REV., vol. 32, 2003, pages 170-180, XP002328264
- D7: WO 01/72926 A (ISIS INNOVATION LIMITED; SHCHEPINOV, MIKHAIL SERGEEVICH; SOUTHERN, EDW) 4 October 2001 (2001-10-04)
- D8: WO 99/60007 A (ISIS INNOVATION LIMITED; SOUTHERN, EDWIN, MELLOR; SHCHEPINOV, MIKHAIL,) 25 November 1999 (1999-11-25)
- D9: WO 98/20019 A (SEQUENOM, INC; LOUGH, DAVID, M; KOESTER, HUBERT; REUTER, DIRK; HIGGINS) 14 May 1998 (1998-05-14)
- D10: EP-A-0 424 819 (MILLIPORE CORPORATION) 2 May 1991 (1991-05-02)
- D11: US 2003/119021 A1 (KOSTER HUBERT ET AL) 26 June 2003 (2003-06-26)

The method of claims 1, 2, 8, 9 and 15 involving the formation of trityl ions is not new in the light of D11 which discloses the capture of proteins by functionalised trityl-based capture reagents, optionally on a support, and their subsequent MS-analysis, preferably by MALDI (see example 9; fig. 15, 20; the claims).

The biopolymer of claims 3 and 4 is not new in view of D3, p. 6915, D11 (example 9), and D6 (scheme 8).

Claim 5 is related to an unstable chemical entity, an ion having certain structural features. Unstable compounds are not deemed susceptible to industrial application for obvious reasons. Claim 5 will therefore not be examined with respect to novelty and inventive step.

The compounds of claim 6 and 7 are not new, see D1, D2, D4, D5, D6, D7, D8, D10, D11. The relevant passages of the documents are indicated in the search report.

A solid support (IVaiii) according to claim 11 is not new in view of D9 (fig. 3; 10 - see also page 19 of this application: M in (IVaiii) can have the meaning OR or halo). Further novelty-destroying subject-matter can be found in D3, p. 6914, compound 1, D7 (scheme 2) and D6 (scheme 9).

A solid support (IVai) according to claim 11 is not new in view of D2 (scheme II) and D8 (fig. 3).

A support according to claim 12 comprising biomolecules linked to trityl moieties by suitable functional groups is disclosed in D11 (fig. 15; claim 11).

Thus, all independent claims are not new.

The dependent claims that appear to be novel (claims 30-42) appear not to comprise subject-matter involving an inventive step.

Re Item VIII

Certain observations on the international application

The claims do not meet the requirements of Article 6 PCT for the following reasons:

Claims 3 and 4 describe the same class of compounds by different formulae. Only the formula given in claim 3 appears appropriate. Claim 4 appears therefore superfluous. Should some of the claimed compounds exist in the form of salts as indicated in claim 4, the corresponding structural features of this limited group of compounds should be given in the claim. The same observations apply to compound claims 6, 7 and to method claims 8, 9 and 1, 2.

The nature of the bonds between support and trityl moiety is not defined in the claims mentioning the support. Claims 8-12 therefore lack clarity.

Claims 15 and 16 relate essentially to the same subject-matter. The claims taken as a whole are not concise.